AMENDMENTS TO THE SPECIFICATION

Please replace the sequence listing submitted September 23, 2004 for insertion on page 66 of the specification before the claims with the sequence listing being submitted with this Amendment.

Please replace the paragraph beginning on page 18, line 7, and ending on page 19, line 9, with the following paragraph:

In a third approach, the assay distinguishes the fragment (or fragments) based on one or more epitopes in thrombospondin that are not present in the fragment. As an illustrative but not restrictive example, an epitope shared by thrombospondin and a thrombospondin fragment is used to obtain a quantitation of a total, thrombospondin plus thrombospondin fragment(s), from which is then subtracted a quantitation of thrombospondin obtained using an epitope present in thrombospondin but not present in a fragment. The difference between the two quantitations is a quantitation of the amount of fragment. As an example, epitopes in thrombospondin but not in at least one fragment from the group of an 80 to 140 kDa, a 40 to 55 kDa, or a 20 to 35 kDa fragment present in plasma can be selected from the group consisting of an epitope from outside the protease-resistant central core domain, an epitope in the N-terminal domain, an epitope in the N-terminal heparin-binding domain, a heparin-binding sequence in the N-terminal domain, a heparin-binding sequence in the N-terminal domain selected from the group consisting of residues 23-32 (RKGSGRRLVK; SEQ ID NO:59), residues 23-29 (RKGSGRR; SEQ ID NO:60), and residues 77-83 (RQMKKTR; SEQ ID NO:61) of the mature protein (see Chapter 2, "The primary structure of the thrombospondins" in The Thrombospondin Gene Family by JC Adams, RP Tucker, & J Lawler, Springer-Verlag: New York, 1995, pp. 11-42, but especially p. 13 & Table 2.1; Chapter 6, "Mechanistic and functional aspects of the interactions of thrombospondins with cell surfaces," *ibidem* pp. 105-157, but especially pp. 108 & 114; Lawler J et al. Expression and mutagenesis of thrombospondin. Biochemistry. 1992 Feb 4;31(4):1173-80; and Cardin AD & Weintraub HJ. Molecular modeling of protein-glycosaminoglycan

interactions. Arteriosclerosis. 1989 Jan-Feb;9(1):21-32), a heparin-binding sequence in the N-terminal domain selected from the group consisting of residues 22-29 (ARKGSGRR; SEQ ID NO: 62), residues 79-84 (MKKTRG; SEQ ID NO: 63), and residues 178-189 (RLRIAKGGVNDN; SEQ ID NO: 64) of the mature protein (reviewed in the Discussion section of Voland C et al.: Platelet-osteosarcoma cell interaction is mediated through a specific fibrinogen-binding sequence located within the N-terminal domain of thrombospondin 1. J Bone Miner Res. 2000 Feb;15(2):361-368), an epitope in the C-terminal domain, an epitope in the C-terminal cell-binding domain, a thrombospondin epitope not found in a plasma fragment, a thrombospondin epitope not found in a plasma fragment of 80 to 140 kDa, a thrombospondin epitope not found in a plasma fragment of 40 to 55 kDa, and a thrombospondin epitope not found in a plasma fragment of 20 to 35 kDa, where all kDa molecular weights are those after reduction. It is understood that the absence of a strong, functional heparin-binding domain from a thrombospondin fragment in plasma will be a factor allowing its accumulation in plasma (many heparin- or heparan-binding proteins are cleared from plasma very quickly; see for example, Wallinder L et al. Rapid removal to the liver of intravenously injected lipoprotein lipase. Biochim Biophys Acta. 1979 Oct 26;575(1):166-73).

Please replace the paragraph beginning on page 25, line 7, and ending on page 25, line 21, with the following paragraph:

Raising conventional antibodies (also referred to herein simply as "antibodies" as opposed to "single chain antibodies"; and an example of a conventional antibody is IgG, which is composed of two heavy chains and two light chains) is merely one of a number of methods that are generally based on the approach of random, semi-random, directed, combinatorial, and/or other means for the generation of large numbers of diverse peptides and/or non-peptides, that is then followed by a selection procedure to identify within this large number those peptides and/or non-peptides that bind to a target and/or an epitope within a target. Selection can then be followed by methods for improving the peptides and/or non-peptides to achieve better affinity and/or specificity. These diverse peptides and/or non-peptides may be conventional multi-chain

antibodies (polyclonal or monoclonal), single-chain antibodies, or non-antibodies, including but not limited to peptides, products of phage display, aptamers, DNA, RNA, or modified DNA or RNA. Also contemplated are thrombospondin receptors and/or binding proteins (such as a CSVTCG (SEQ ID NO:54) receptor, a CSVTCG (SEQ ID NO:54) binding molecule, CD36, angiocidin, 26S proteasome non-ATPase regulatory subunit 4, and/or anti-secretory factor).

Please replace the paragraph beginning on page 36, line 20 and ending on page 36, line 28, with the following paragraph:

Such kits wherein said protein non-antibody is selected from the group consisting of a thrombospondin receptor, a thrombospondin receptor that binds within a protease-resistant core region, a thrombospondin receptor that binds a TSP fragment present in the plasma of a cancer patient, a CSVTCG (SEQ ID NO:54) receptor, a CSVTCG (SEQ ID NO:54) binding molecule, a CD36 (which reportedly binds CSVTCG (SEQ ID NO:54); see Carron JA et al., A CD36-binding peptide from thrombospondin-1 can stimulate resorption by osteoclasts in vitro. Biochem Biophys Res Commun. 2000 Apr 21;270(3):1124-7), angiocidin, anti-secretory factor, 26S proteasome non-ATPase regulatory subunit 4, fragments thereof that bind to their respective targets, and combinations, chimeras, and recombinant versions of said receptors and fragments.

Please replace the paragraph beginning on page 37, line 1 and ending on page 37, line 19, with the following paragraph:

A kit for the determination of the presence of, and/or the amount of, and/or the concentration of, one or more thrombospondin fragments in a material taken or gathered from an organism, said kit comprising a binding agent that will react with thrombospondin but not with a fragment of interest. Particular embodiments are:

Such kits wherein said binding agent comprises a protein;

Such kits wherein said protein comprises an antibody;

Such kits wherein said antibody is a monoclonal antibody or a polyclonal antibody;

Such kits wherein said protein comprises a fragment of an antibody;

Such kits wherein said protein comprises a single-chain antibody;

Such kits wherein said single chain antibody is derived from a phage display library;

Such kits wherein the protein is a non-antibody, the non-antibody being a protein that is neither an antibody nor a single-chain antibody;

Such kits wherein said non-antibody is selected from the group consisting a an integrin, an RGD receptor, an RFYVVMWK (SEQ ID NO:55) receptor, an RFYVVM (SEQ ID NO:56) receptor, an FYVVMWK (SEQ ID NO:57) receptor, an IRVVM (SEQ ID NO:58) receptor, fragments thereof that bind to their respective targets, and combinations, chimeras, and recombinant versions of said receptors, integrins, and fragments; and

Such kits wherein said binding agent comprises an aptamer, meaning a DNA or RNA or related compound, that binds thrombospondin or a thrombospondin fragment.